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Research Article

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UNUSUAL AND RARE PRESENTATION OF HYPOTHYROIDISM (HOFFMAN SYNDROME)

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ABSTRACT

The neurological manifestations of hypothyroidism are very unusual to see as initial symptoms and they usually occur late in the course of disease. Muscle hypertrophy is an extremely rare finding in hypothyroid patients. Hypothyroidism presenting as muscle stiffness and muscle pseudo hypertrophy in adults is known as Hoffmann's syndrome. Laboratory investigation in hypothyroid myopathy generally shows increased levels of muscle enzyme. The electrophysiological study may reveal features suggestive of myopathy, neuropathy or mixed pattern. The symptoms and also the serum levels of enzymes return to normal with hormone replacement therapy. We report a case of hypothyroidism with calf muscle hypertrophy.

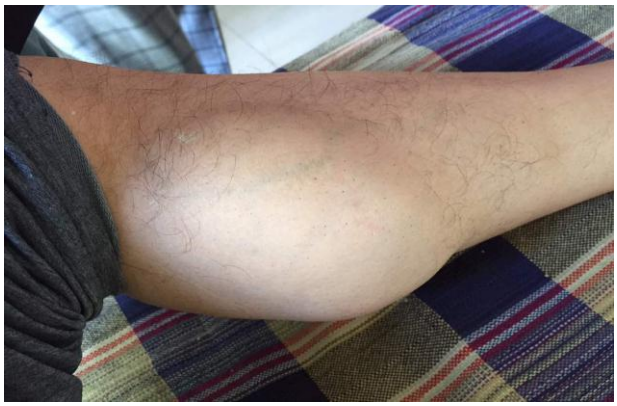
KEYWORDS: Pseudohypertrophy, coarse skin, hoarse voice.

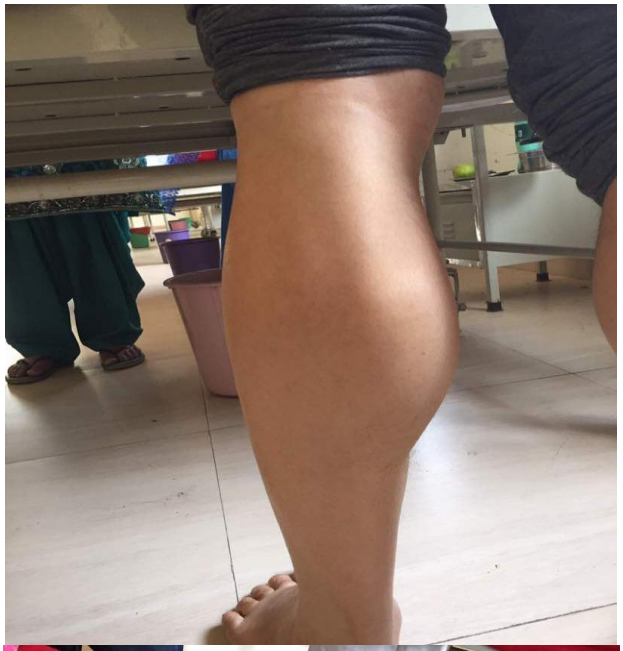
INTRODUCTION

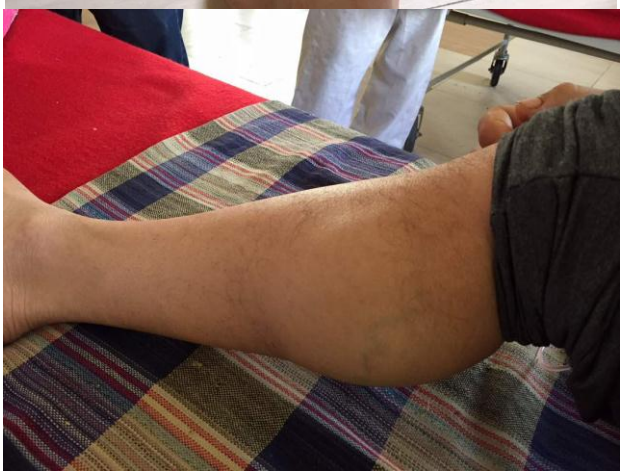
The common symptoms of myopathy due to hypothyroidism are proximal muscle weakness, muscle cramps, myxoedema on percussion, delay in deep tendon reflexes and rarely development of muscle hypertrophy.[1] Severity of myopathy generally correlates with the duration and the degree of thyroid hormone deficiency. Hoffmann's syndrome is a rare specific form of hypothyroid myopathy, which causes proximal muscle weakness and hypertrophy of muscles. The muscular hypertrophy with muscle stiffness is reported in less than 10% of hypothyroid patients.[2] The hypothyroidism presenting with initial neurological manifestations is very unusual and rare. Hoffman's syndrome is a specific, rare form of hypothyroid myopathy, which causes proximal weakness and pseudohypertrophy of muscles. It was first described in 1897 in an adult who developed muscle stiffness and difficulty in relaxation of muscles after thyroidectomy.[1] Similar presentation in children with cretinism is referred as Kocher-Debré-Sémélaigne syndrome.[2] We discuss a case of hypothyroid male with this unusual and rare presentation.

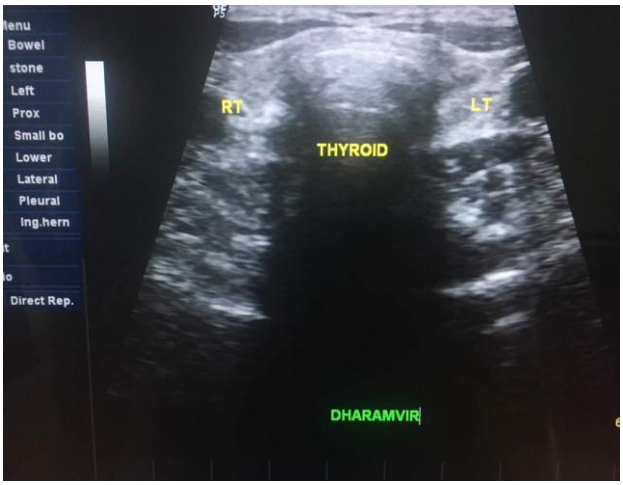
A 30-year-old male presented with complaints of Fatigability, Hoarseness of voice and bilateral hypertrophy of calf muscles for the last 8 months. He had no difficulty in getting up from squatting position and climbing stairs. No H/O muscular cramps and stiffness and pain in muscles. There was no history of bladder or bowel involvement. There was no history of hypertension, diabetes, or any other chronic illness. There was no history of any prolonged drug intake. On examination, he was found to have periorbital puffiness. He also had a large tongue and hoarseness of voice with coarse and rough skin. He had a pulse rate of 56/min and his blood pressure was 120/80 mm Hg. Evaluation of cardiovascular and respiratory systems did not reveal any significant abnormality. Positive findings from neurological evaluation was hypertrophy of bilateral calf muscles (gastrocnemius) without any associated tenderness [Figures 1-6]. No hypertrophy of thigh, arm, or any other muscle group was noted. There was classical delayed relaxation of bilateral ankle jerks. Laboratory investigation revealed a T3 level of 0.13 ng/ml (normal range: 0.80- 2.0ng/ml), T4 level of 0.420µg/dl (normal range: 5.1-14.10µg/dl), and the activity of thyroid stimulating hormone (TSH) to be 439.1 µIU/ml (normal range: 0.3-5.5 µIU/ml).{Fig 7] Anti-thyroid peroxidase (anti-TPO) antibody was positive. Creatine phosphokinase (CPK) level was 567 IU/l (normal level: <170 U/l). Hemogram revealed mild anemia[8.8gm/dl. Blood sugar[116mg/dl] and liver

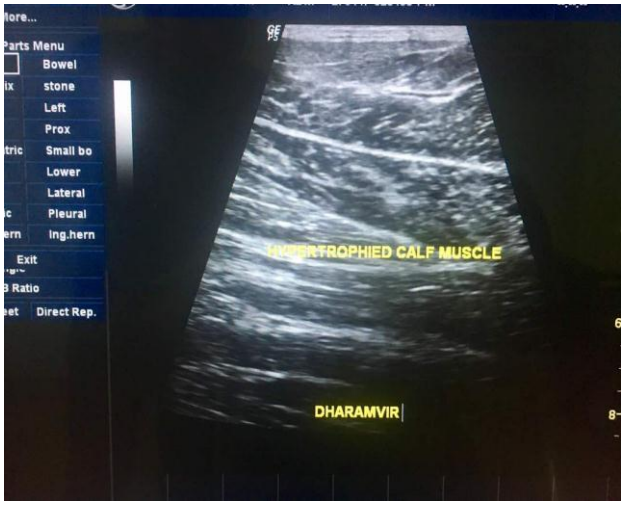
function tests SGOT/SGPT583/221. Blood urea and serum creatinine[urea 22mg/dl creatinine 0.84] were normal. Urine examination was normal and myoglobinuria was absent. Lipid profile evaluation showed hypercholesterolemia (240 mg/dl) and hypertriglyceridemia (180 mg/dl). Electrocardiography (ECG) showed low-voltage complexes and sinus bradycardia potential. Based on the above findings, a diagnosis of Hoffman's syndrome was made. The patient was administered a starting dose of 150 µg/day of levothyroxine. On a routine follow-up later, his symptoms had improved though complete resolution of symptoms had not taken place. The calf hypertrophy, however, still persisted.







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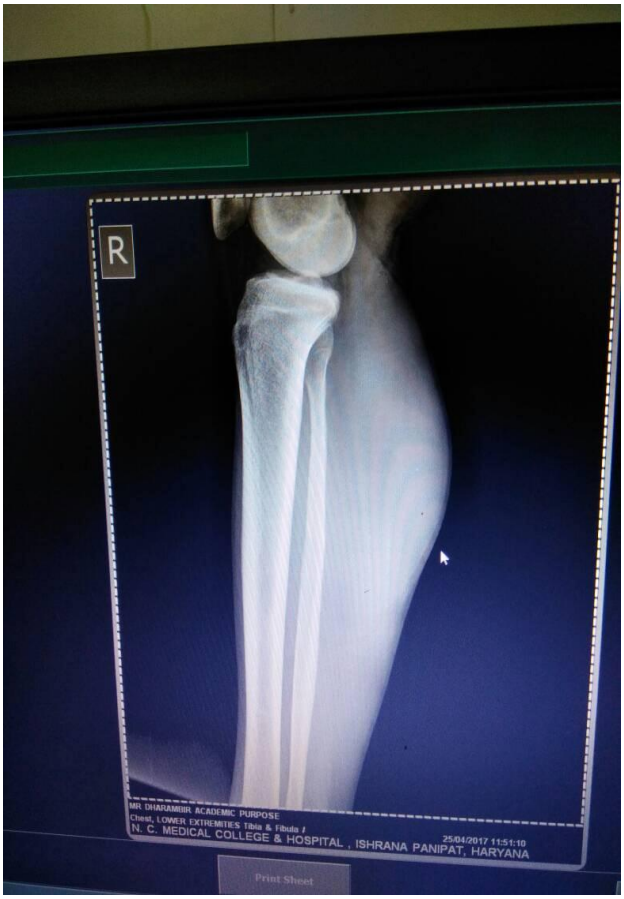
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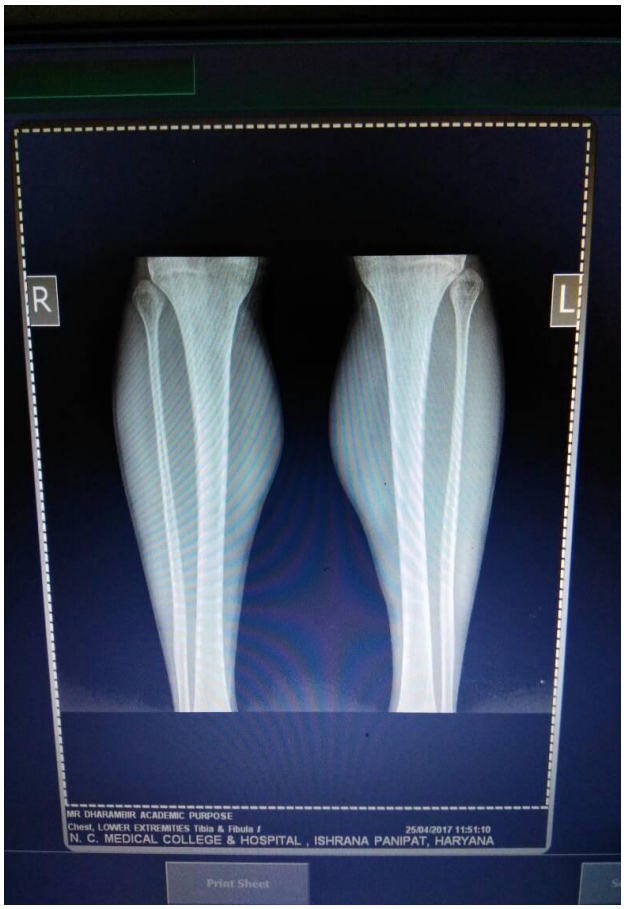
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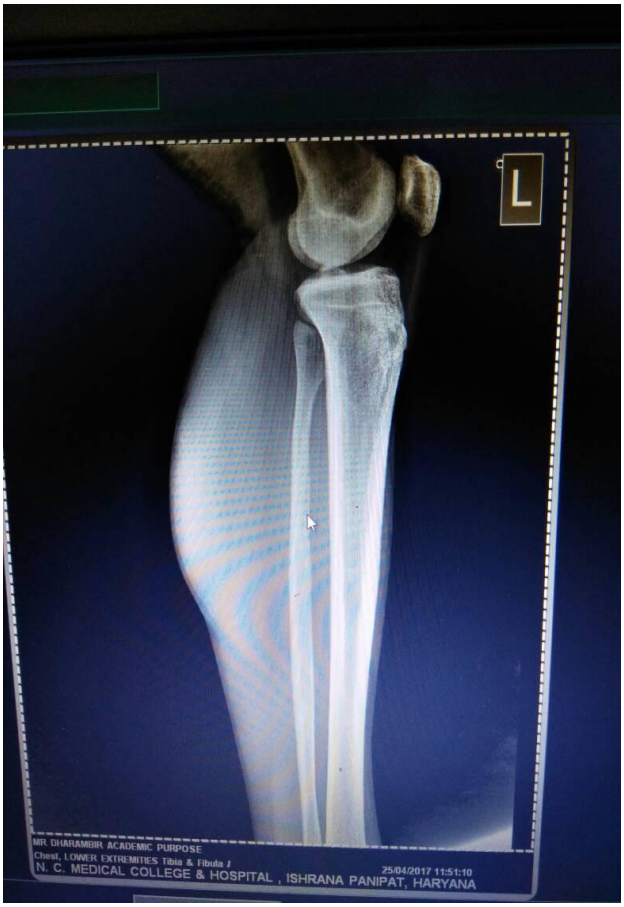
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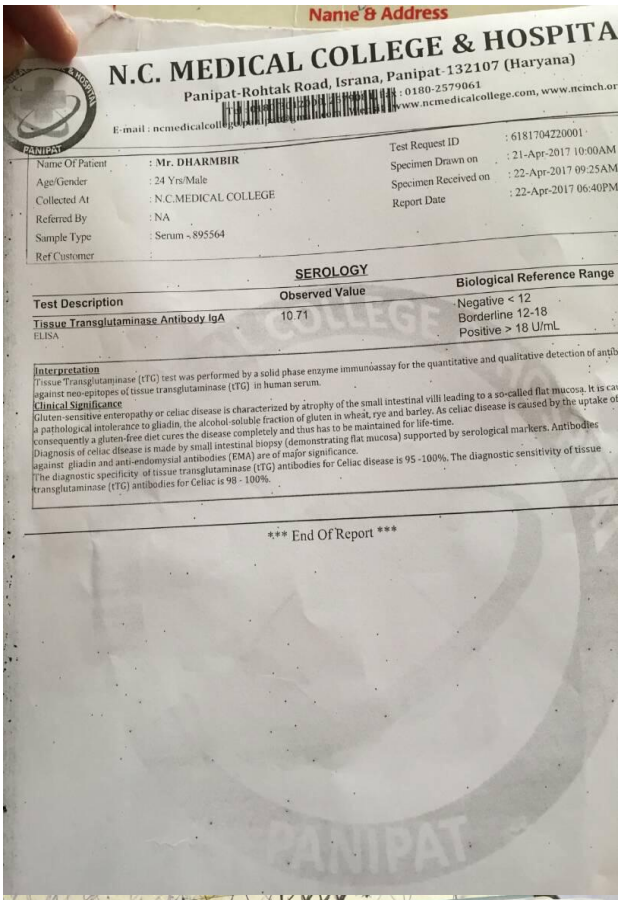

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: 0180-2579061 www.ncmedicalcollege.com, www.ncmch.or

E-mail : ncmedicalcolleg

Name Of Patient	: Mr. DHARMBIR	Test Request ID	: 6181704220001
Age/Gender	: 24 Yrs/Male	Specimen Drawn on	: 21-Apr-2017 10:00AM
Collected At	: N.C.MEDICAL COLLEGE	Specimen Received on	: 22-Apr-2017 09:25AM
Referred By	: NA	Report Date	: 22-Apr-2017 06:40PM
Sample Type	: Serum - 895564		
Ref Customer	:		

SEROLOGY

Test Description	Observed Value	Biological Reference Range
Tissue Transglutaminase Antibody IgA ELISA	10.71	Negative < 12 Borderline 12-18 Positive > 18 U/mL

Interpretation

Tissue Transglutaminase (tTG) test was performed by a solid phase enzyme immunoassay for the quantitative and qualitative detection of antib against neo-epitopes of tissue transglutaminase (tTG) in human serum.

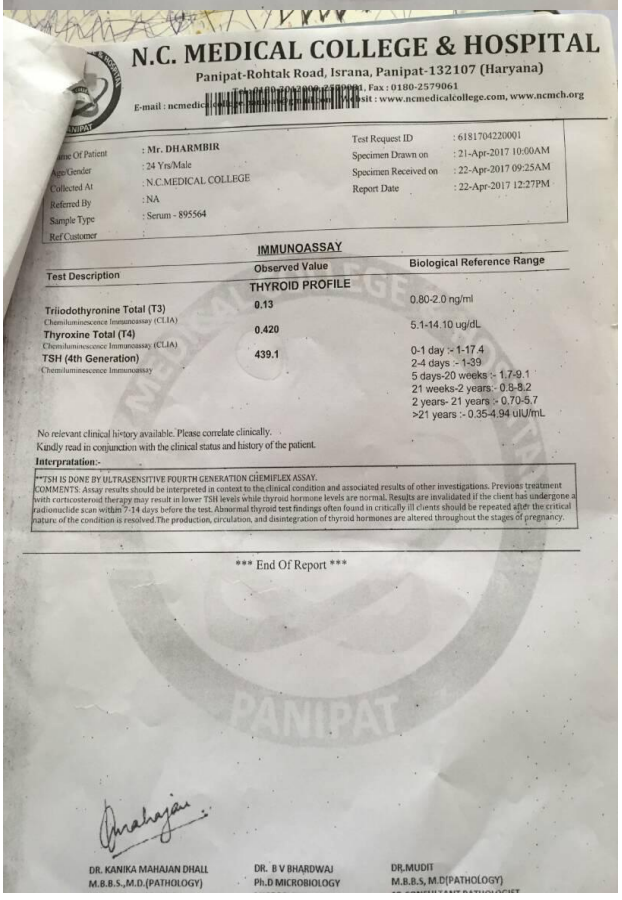
Clinical Significance

Gluten-sensitive enteropathy or celiac disease is characterized by atrophy of the small intestinal villi leading to a so-called flat mucosa. It is ca a pathological intolerance to gliadin, the alcohol-soluble fraction of gluten in wheat, rye and barley. As celiac disease is caused by the uptake of consequently a gluten-free diet cures the disease completely and thus has to be maintained for life-time.

Diagnosis of celiac disease is made by small intestinal biopsy (demonstrating flat mucosa) supported by serological markers. Antibodies against gliadin and anti-endomysial antibodies (EMA) are of major significance.

The diagnostic specificity of tissue transglutaminase (tTG) antibodies for Celiac disease is 95 -100%. The diagnostic sensitivity of tissue transglutaminase (tTG) antibodies for Celiac is 98 - 100%.

*** End Of Report ***



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Name Of Patient	: Mr. DHARMBIR	Test Request ID	: 6181704220001
Age/Gender	: 24 Yrs/Male	Specimen Drawn on	: 21-Apr-2017 10:00AM
Collected At	: N.C.MEDICAL COLLEGE	Specimen Received on	: 22-Apr-2017 09:25AM
Referred By	: NA	Report Date	: 22-Apr-2017 12:27PM
Sample Type	: Serum - 895564		
Ref Customer	:		

IMMUNOASSAY

Test Description	Observed Value	Biological Reference Range
THYROID PROFILE		
Triiodothyronine Total (T3) Chemiluminescence Immunoassay (CLIA)	0.13	0.80-2.0 ng/ml
Thyroxine Total (T4) Chemiluminescence Immunoassay (CLIA)	0.420	5.1-14.10 ug/dL
TSH (4th Generation) Chemiluminescence Immunoassay	439.1	0-1 day :- 1-17.4 2-4 days :- 1-39 5 days-20 weeks :- 1.7-9.1 21 weeks-2 years :- 0.5-8.2 2 years- 21 years :- 0.70-5.7 >21 years :- 0.35-4.94 uIU/mL

No relevant clinical history available. Please correlate clinically.

Kindly read in conjunction with the clinical status and history of the patient.

Interpretation:-

**TSH IS DONE BY ULTRASENSITIVE FOURTH GENERATION CHEMIFLEX ASSAY.

COMMENTS: Assay results should be interpreted in context to the clinical condition and associated results of other investigations. Previous treatment with corticosteroid therapy may result in lower TSH levels while thyroid hormone levels are normal. Results are invalidated if the client has undergone a radionuclide scan within 7-14 days before the test. Abnormal thyroid test findings often found in critically ill clients should be repeated after the critical nature of the condition is resolved.The production, circulation, and disintegration of thyroid hormones are altered throughout the stages of pregnancy.

*** End Of Report ***

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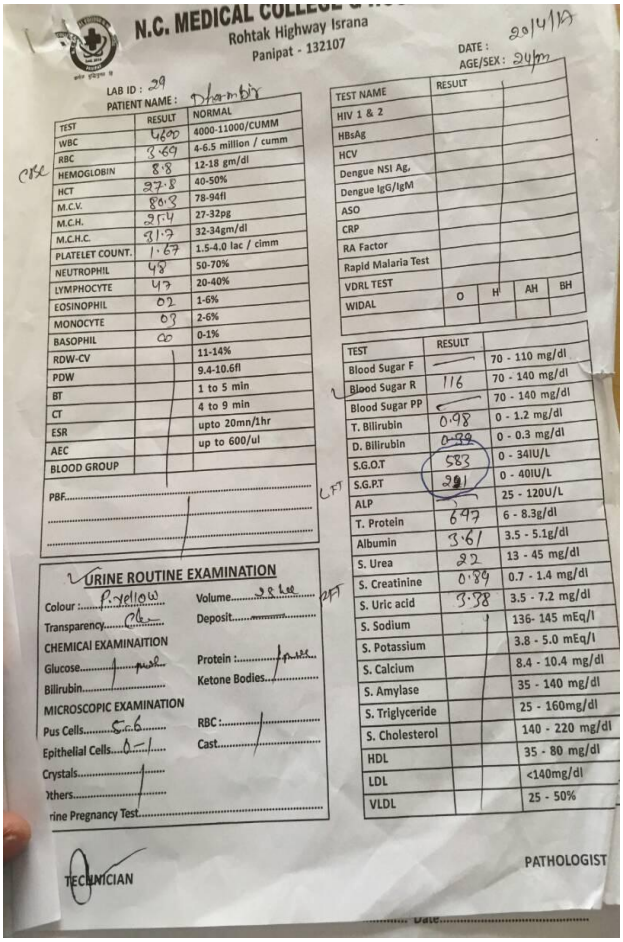
DR. B V BHARDWAJ Ph.D MICROBIOLOGY

DR.MUDIT M.B.B.S, M.D(PATHOLOGY)



N.C. MEDICAL COLLEGE

Rohtak Highway Israna

Panipat - 132107

DATE : 20/4/17

AGE/SEX : 24yrs

LAB ID : 39

PATIENT NAME : Dharmbir

TEST	RESULT	NORMAL
WBC	4600	4000-11000/CUMM
RBC	3.69	4-6.5 million / cumm
HEMOGLOBIN	8.8	12-18 gm/dl
HCT	27.8	40-50%
M.C.V.	80.3	78-94fl
M.C.H.	29.4	27-32pg
M.C.H.C.	31.7	32-34gm/dl
PLATELET COUNT.	1.67	1.5-4.0 lac / cimm
NEUTROPHIL	48	50-70%
LYMPHOCYTE	47	20-40%
EOSINOPHIL	02	1-6%
MONOCYTE	03	2-6%
BASOPHIL	00	0-1%
RDW-CV		11-14%
PDW		9.4-10.6fl
BT		1 to 5 min
CT		4 to 9 min
ESR		upto 20mn/1hr
AEC		up to 600/ul
BLOOD GROUP		

PBF.....

TEST NAME	RESULT
HIV 1 & 2	
HBsAg	
HCV	
Dengue NSI Ag.	
Dengue IgG/IgM	
ASO	
CRP	
RA Factor	
Rapid Malaria Test	
VDRL TEST	
WIDAL	O H AH BH

TEST	RESULT	
Blood Sugar F		70 - 110 mg/dl
Blood Sugar R	116	70 - 140 mg/dl
Blood Sugar PP		70 - 140 mg/dl
T. Bilirubin	0.98	0 - 1.2 mg/dl
D. Bilirubin	0.39	0 - 0.3 mg/dl
S.G.O.T	583	0 - 34IU/L
S.G.P.T	281	0 - 40IU/L
ALP	647	25 - 120U/L
T. Protein	3.61	6 - 8.3g/dl
Albumin	22	3.5 - 5.1g/dl
S. Urea	0.89	13 - 45 mg/dl
S. Creatinine	3.58	0.7 - 1.4 mg/dl
S. Uric acid		3.5 - 7.2 mg/dl
S. Sodium		136- 145 mEq/l
S. Potassium		3.8 - 5.0 mEq/l
S. Calcium		8.4 - 10.4 mg/dl
S. Amylase		35 - 140 mg/dl
S. Triglyceride		25 - 160mg/dl
S. Cholesterol		140 - 220 mg/dl
HDL		35 - 80 mg/dl
LDL		<140mg/dl
VLDL		25 - 50%

URINE ROUTINE EXAMINATION

Colour : P.yellow Volume : 30 Lac

Transparency : Clear Deposit :

CHEMICAL EXAMINAITION

Glucose : nil Protein : trace

Bilirubin : Ketone Bodies :

MICROSCOPIC EXAMINATION

Pus Cells : 5-6 RBC :

Epithelial Cells : 0-1 Cast :

Crystals :

Others :

Urine Pregnancy Test :

TECHNICIAN

PATHOLOGIST

Date :

DISCUSSION

The neurological manifestations of hypothyroidism usually occur later, and it is unusual that they are found as initial symptoms.[3,4] Muscular symptoms are common in hypothyroid patients (varying from myalgia, weakness, stiffness, cramps, and easy fatigability in 30-80% of the patients).[3,5] The common symptoms of myopathy due to hypothyroidism are proximal muscle weakness, muscle cramps, myxedema on percussion, delay in deep tendon reflexes, and rarely, development of muscle hypertrophy.[6] The muscular hypertrophy with muscle stiffness is reported in less than 10% of hypothyroid patients.[3,5] Although any muscle could be affected, the predominant muscles showing such changes are thigh, leg, arm, and tongue.[3] Hypertrophy of gastrocnemius is also frequently seen.[3] Similar presentation of calf muscle hypertrophy with weakness is also seen in Duchenne and Becker muscle dystrophy, focal myositis, sarcoid granulomas, and amyloid deposits in muscles. The CPK level is elevated in thyroid myopathy and is very high in some patients (10-100 times greater than the normal level); however, it has no correlation with weakness.[7] One infrequent, but potentially life-threatening complication of hypothyroid myopathy is rhabdomyolysis. It can lead to acute renal failure if not managed promptly. Some common precipitating factors are severe exercise, trauma, alcohol intake, and electrolyte imbalance.[8]

Thyroid hormones significantly influence cellular metabolism. So, their deficiency results in significant impairment of normal cellular functions. A reduction in muscle mitochondrial oxidative capacity and beta-adrenergic receptors, as well as the induction of an insulin-resistant state, may result in these changes.[6] The muscle involvement in hypothyroidism is caused by changes in muscle fibers from fast-twitching type II to slow-twitching type-I fibers.[2,3] This results in slowness of muscle contraction associated with hypothyroidism. The exact cause of hypertrophy remains obscure, but it could be due to an increase in connective tissue and increase in size and number of muscular fibers.[3,4] On histopathologic examination, the muscles appear pale and swollen. The muscle fibers may show swelling, loss of normal striations, and separation by mucinous deposits.[2] The accumulation of glycosaminoglycans in muscles could also contribute to the hypertrophy.[3] Delayed relaxation of deep tendon reflexes is due to impaired calcium sequestration by sarcoplasmic reticulum, which prolongs twitch duration.

Hypothyroidism is a very common endocrine disease and clinicians should be aware of this atypical and rare presentation of hypothyroid disease spectrum. Hoffman's syndrome represents those few forms of myopathy that completely reverse on prompt therapy and, hence, has a good outcome.

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